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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,563	10/23/2001	Mary Theresa Murray	3087.00007	7737

7590 07/01/2004

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,563	MURRAY ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *9-20 and 27-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 4/23/04.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-8 and 21-24) in the reply filed on 4/23/04 is acknowledged. The traversal is on the ground(s) that all claims are related and are grouped in the same or similar classes and/or subclasses. Therefore, applicants assert, it would not be a serious burden to search all the claims. This is not found persuasive because as indicated in the restriction requirement, the searches required for each group is not co-extensive with the searches required for the other groups. Evidence previously presented as prima facie evidence of a serious search burden is different class/sub-classifications as well as different search terms required for the different groups.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9-20 and 27-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/23/04.

Therefore, claims 9-20 and 27-42 have been withdrawn from consideration and claims 1-8 and 21-26 are examined herein.

Claim Objections

Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim does not further limit the dependent claim because the instant claim is drawn to the method of claim 1 wherein said delivering step includes delivery of **exogenous** mRNA. It is noted that the generally accepted definition for the term "exogenous" is anything that is not endogenous (i.e. not inside a cell). Therefore, with respect to the phrase exogenous mRNA, the phrase indicates that mRNA outside the cell is delivered to the cell. However, since claim 1 is already drawn to a method wherein a mRNA is delivered to a cell—delivering a mRNA to a cell must mean an mRNA outside the cell is delivered to the cell. Any other interpretation would require delivering a mRNA that is already inside the cell to the cell, which would render the claim indefinite as it would be unclear how a mRNA that is already inside a cell could be delivered to the cell.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is drawn to the method of claim 6 wherein said increasing step includes intracellularly delivering mRNA mRNA encoding a translational regulatory protein to increase protein synthesis from endogenous **protein** in the cells. It is unclear how protein synthesis can be increased from endogenous protein in the cells as protein synthesis is from mRNA, not protein. It is noted that claim 8 depends on claim 7 and is therefore rejected for the same reason.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a written description rejection.**

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between

function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164)

In the instant case the claims encompass "mRNA functionally related to protein synthesis" as well as "mRNA functionally related to protein synthesis" (see claims 1 and 5). Looking to the specification for guidance, it is noted that page 11 of the specification indicates:

> "The mRNA of the present invention functionally relates to protein synthesis. More specifically, the mRNA encodes for proteins that are desired to be upregulated in a cell. In other words the mRNA encodes proteins that are required to be expressed in a cell. For example, the mRNA can encode for proteins necessary for wound healing, to promote cell death, or any other desired effect that is based upon or relies upon protein synthesis."

Based in this definition, the claims encompass a genus of molecules wherein the genus comprises thousands, possibly millions of different mRNAs considering that the genus encompasses all mRNAs encoding "proteins that are desired to be upregulated in a cell", and including "any other desired effect that is based upon or relies upon protein synthesis." As such the claims encompass mRNAs that are not described in the specification. Furthermore, applicants have not disclosed any structural elements that are common to all members of the genus and wherein that structure confers the desired function to the molecules having that structure. That is, applicants have not described any structure-function relationship for the members of the genus. As such, the specification has not adequately described a representative number of species, and thus the written description requirement has not been met.

Additionally, claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement in view of the written description rejection set forth above. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As mentioned above, the claims encompass mRNAs for which there insufficient written description provided in the specification. Without a clear indication of the mRNA sequences encompassed by the claims, one of skill in the art would not know how to make or use the claimed invention without performing an undue amount of additional experimentation.

Claims 6-8 and 21-24 rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The claims are drawn to methods wherein method steps that are critical or essential to the practice of the invention are not included in the claim(s). Therefore, the incomplete claims are not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Specifically, claim 6 is drawn to a method of augmenting transient protein synthesis in cells in need of increased protein synthesis by increasing protein synthesis from endogenous cellular mRNA in the cells. However, the claim does not include the method steps for increasing the protein synthesis in the cells, and in order to be able to use the claimed method, the required steps must be indicated in the claim. Claims 7 and 8 are rejected for being dependent on claim 6.

Claim 21 is drawn to a method of augmenting wound healing in cells by increasing protein synthesis from endogenous cellular mRNA in the wound. However, the claim does not include the method steps for increasing the protein synthesis in the wound, and in order to be able to use the claimed method, the required steps must be indicated in the claim. Claims 22-24 are rejected for being dependent on claim 21.

Claims 1-8 and 21-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for augmenting the healing of a wound in a subject having said wound by administering mRNA encoding a growth factor either alone or in combination with a mRNA encoding eIF4e directly to cells of the wound, wherein administering said mRNA(s) to said cells transiently increases protein synthesis of said growth factors in said cells resulting in augmenting the healing of said wound;

does not reasonably provide enablement for the full scope encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The nature of the claims is increasing protein synthesis in a cell by administering mRNAs encoding a protein whose increased synthesis is desired, or administering mRNAs encoding factors that increase protein synthesis the cell, or administering both mRNAs (i.e. mRNAs encoding a protein whose increased synthesis is desired AND mRNAs encoding factors that increase protein synthesis the cell).

The breadth of the claims

The claims are very broad and encompass increasing the expression of any mRNA in a cell for any reason. As such, the claims encompass a very wide array of patently distinct methods such as: methods for augmenting wound healing by administering specific mRNAs encoding polypeptides that wither directly or indirectly increase the synthesis of proteins that result in increased wound healing; as well as methods of decreasing the growth of a population of cells by administering mRNAs encoding polypeptides that either directly or indirectly inhibit cell growth; as well as increasing the synthesis of any protein in a cell (for any reason) by administering a mRNA encoding a factor that is involved in increasing protein synthesis in general to the cell. Therefore, in the most general sense, the claims encompass a method for increasing protein synthesis (e.g., of any desired protein) in a cell by administering mRNA encoding a polypeptide that increases protein synthesis in the cell, wherein the mRNA can encode the desired protein itself or a factor that increases the synthesis of the desired protein such as a translational regulatory protein or any other protein that would increase the expression of the desired protein (e.g., a transcription factor).

The unpredictability of the art and the state of the prior art

As indicated above, the claims are incredibly broad and encompass a myriad of different methods wherein all of the methods involve increasing protein synthesis in a cell by administering to the cell mRNA encoding a polypeptide that increases protein synthesis in the cell. The claims are so broad that they encompass a number of patentably distinct methods (note since the methods use different reagents (such as different mRNAs) and have different desired effect (such as increasing cell growth or decreasing cell growth as indicated above) the methods

encompassed by the claims are patentably distinct. However, although the methods encompassed by the generic claim include methods with such drastically different desired outcomes (e.g., cell growth vs. cell death), all of the claims encompass increasing protein synthesis in a cell by administering to the cell a mRNA encoding a factor involved in protein synthesis (e.g., eIF4E, or another translation regulatory factor). Therefore, the claims, given their broadest reasonable interpretation encompass both increasing cell growth (e.g., augmenting wound healing by increasing the synthesis of growth factors) as well as inhibiting cell growth (e.g. by increasing the synthesis of apoptotic factors) by administering a mRNA that encodes a factor that increases protein synthesis in general (e.g., eIF4e). Obviously, it is unclear how a method that merely encompasses administering a mRNA that encodes a factor the increases protein synthesis can result in cell growth AND cell death.

It is known in the prior art that administering mRNA encoding the growth factor EGF can be administered to wound cells and result in the transient increase in synthesis of the growth factor in the cells which leads to faster wound healing (e.g., see Sohn et al. Wound Rep. Reg, 2001, cited in the IDS). Also methods for increasing wound healing wherein DNA encoding EGF was administered to wound cells was also known in the art (e.g., see Andree et al.-cited in IDS). Furthermore, translation regulatory proteins which increase the synthesis proteins in a cell were also known in the art (e.g., see Hiremath et al.—cited in IDS). However, it has also been shown that overexpression of certain translation factors (e.g., eIF4E) transformed normal cells into cancerous cells (e.g., see Lazaris-Karatzas—cited in the IDS). Therefore, the prior art indicates that simply increasing the synthesis of translational regulatory proteins can turn normal cells into cancerous cells, thus making it unpredictable how a nucleic acid encoding a

translational regulatory protein can be administered to a cell and result in the desired outcome without transforming the cells into cancerous cells.

Working Examples and Guidance in the Specification

The specification indicates by working example a specific method. Specifically, the specification indicates a method that can augment the healing of a wound by administering a mRNA encoding a growth factor (specifically EGF) to the cells of a wound, resulting in increased wound healing. Also disclosed is a method that can augment the healing of a wound by administering a mRNA encoding a growth factor (specifically EGF) in combination with a mRNA encoding the translation initiation factor eIF4E to the cells of a wound, resulting in increased wound healing. It is noted there are no working examples that indicate administering a mRNA encoding a translation regulatory protein to a cell can result such diametrically opposed outcomes such as increasing cell growth and increasing cell death.

Quantity of Experimentation

Considering the breadth of claims (that includes a wide array of patentably distinct methods) and the limited amount of working examples and guidance provided, additional experimentation would be required in order to practice the broadest claimed methods their full scope. For instance, additional experimentation would be required with respect to methods of increasing growth and decreasing growth by administering a mRNA encoding a regulator of translation to a cell.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the breadth of the claims, the teachings of the prior art, the lack of working examples and guidance in the specification, and the high degree of skill required as a whole, it is concluded that the amount of experimentation required to perform the broadly claimed invention to the full scope encompasses by the claims is undue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-6, 21 and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Sohn et al. (Wound Rep. Reg. 2001—cited in IDS).

To the extent that the instant claims are drawn to a method of augmenting transient protein synthesis in a cell by delivering to the cell mRNA that is functionally related to protein synthesis (wherein functionally related to protein synthesis can be any desired protein, as indicated by the specification (see above)), and including methods of augmenting wound healing the instant rejection is proper.

It is noted that the instant claims, given the broadest reasonable interpretation, encompass augmenting transient protein synthesis in a cell by delivering to the cell mRNA encoding the protein whose increased synthesis is desired.

Sohn teaches a method of augmenting wound healing by delivering an exogenous mRNA encoding the growth factor EGF to wound cells using particle acceleration to deliver the mRNA to the cells wherein the method results in an increase of protein synthesis of the mRNA delivered into the cell (which once delivered into the cell is, by definition, endogenous) such that the method results in a transient increase in protein synthesis in the cell and augmenting the helaing of the wound (e.g., see abtract, Table 3, etc.). Therefore, the teachings of Sohn clearly anticipate the instant claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-8656. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0756. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell, Ph.D.
Art unit 1635

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PRIMARY EXAMINER